Inhibitors and Activators

Introduction and Reorientation

Most people can't handle the 1/x thing, so the Lineweaver-Burk plots are great for board fodder. Don't mess it up. We see your challenging-inverted-negative-reciprocal and raise you a we-can-get-you-to-the-right-answer-95%-of-the-time-without-math.

Remember four rules:

1. ↑ on the y-axis = ↓ V_{max}
2. ← on the x-axis = ↓ K_M = ↑ Affinity
3. Competitive inhibition for the binding site affects only K_M
4. Noncompetitive inhibition of the non-binding site affects only V_{max}

Let's Just Get the Graphs Out of the Way

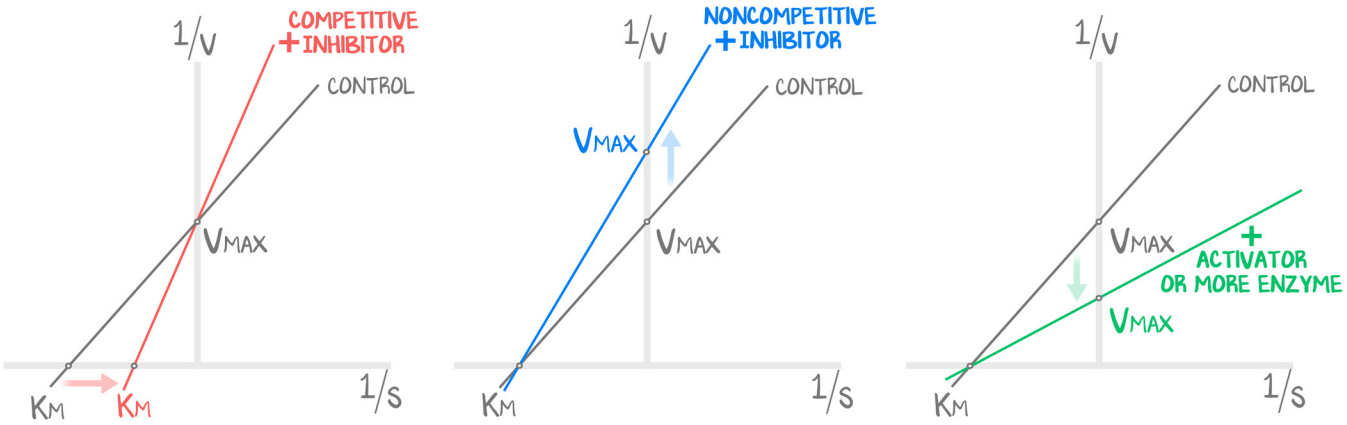

Figure 18.1: Lineweaver-Burk Graphs
Memorize these three graphs, get the question correct.

INTERACTION	K_M	V_{MAX}
Competitive Inhibition	↑ K_M = ↓ affinity . . . so ⟶ x-axis	No change V_{max}
Noncompetitive Inhibition	No change K_M No change affinity	↓ V_{max} . . . so ↑ y-axis
↑ [Enzyme]	No change K_M No change affinity	↑ V_{max} . . . so ↓ y-axis
↑ [Effective] (Activator)	No change K_M No change affinity	↑ V_{max} . . . so ↓ y-axis

Table 18.1

Competitive Inhibition

Competitive inhibition binds to the active binding site of the enzyme. The active binding site can either be occupied by the substrate or the competitor. What this does is effectively reduce the affinity of the enzyme for the substrate (something else has its attention). Affinity affects K_M, the x-axis, and causes no change to the y-axis. **Decreased affinity means move right on the x-axis**. And that is the only movement that occurs. The intersection with the y-axis is the same (no change V_{max}), but the intersection with the x-axis changes, moving closer to the y-axis.

These sorts of inhibitors are **reversible** and can **be outcompeted**. If more substrate is added we can get back to normal V_{max}. Adding substrate for the same V_{max} means that the K_M value will have gone up. K_M going up means lower affinity. K_M going up means it moves to the right.

Noncompetitive Inhibition

Noncompetitive inhibitors bind **irreversibly** to the enzyme and a site that's **not the active binding site**. It's referred to as **allosteric**. If it's bound irreversibly, and can't be outcompeted, as much substrate as desired could be added, yet the enzymes with the inhibitor are effectively removed from the solution. That means the total number of enzymes has gone down. When the effective concentration of enzymes has fallen, it's therefore a fall in V_{max}. A **fall in V_{max}** means a **rise on the y-axis**.

The affinity for the working enzymes remains the same. There's no change to K_M. Only the total number has gone down through the silencing of the enzyme by inhibition. Think of this as the enzymes reaching saturation faster as the number of enzymes has been reduced (they're still there, they just can't do anything).

Activators

Well, if removing the effective number of enzymes decreased V_{max} (up on the y-axis), what happens when we **add enzyme** . . . or . . . more importantly, **noncompetitively excite** the enzyme? Both do the effective opposite of noncompetitive inhibition. They raise the amount of enzyme, either through actual numbers (add enzyme) or by upregulating enzyme function (activators). Regardless, the K_M for the enzyme can't be altered, so K_M stays the same. But as "more enzymes are here" the V_{max} goes up, which means down on the y-axis.